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Search Results -

Terms	Documents
antimuscarinic phospholipid inhaler particle	5

Database: US Patents Full-Text Database; US Pre-Grant Publication Full-Text Database; JPO Abstracts Database; EPO Abstracts Database; Derwent World Patents Index; IBM Technical Disclosure Bulletins

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DATE: Thursday, September 19, 2002 Printable Copy Create Case

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DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=AND			
L5	antimuscarinic phospholipid inhaler particle	5	L5
L4	L3 inhaler	1	L4
L3	L1 phospholipid	36	L3
L2	L1 antimuscarinic	0	L2
L1	"leukotriene receptor antagonist"	145	L1

END OF SEARCH HISTORY

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L3: Entry 12 of 36 File: PGPB Jul 5, 2001

DOCUMENT-IDENTIFIER: US 20010006656 A1
TITLE: METHODS AND COMPOSITIONS FOR INHIBITING INFLAMMATION ASSOCIATED WITH PULMONARY DISEASE

Detail Description Paragraph (47):
[0067] A pharmaceutical composition comprising a HMG-CoA reductase inhibitor also can be incorporated, if desired, into liposomes, microspheres or other polymer matrices (Gregoriadis, Liposome Technology, Vols. I to III, 2nd ed., CRC Press, Boca Raton Fla. (1993)). Liposomes, for example, which consist of phospholipids or other lipids, are nontoxic, physiologically acceptable and metabolizable carriers that are relatively simple to make and administer.

Detail Description Paragraph (57):
[0077] A HMG-CoA reductase inhibitor can be administered in combination with one or more other compounds that are effective at treating inflammation such as other anti-inflammatory agents. A HMG-CoA reductase inhibitor can be administered in combination with steroidal anti-inflammatory agents including corticosteroids, for example, dexamethasone, beclomethasone, fluticasone, triamcinolone and budesonide. A HMG-CoA reductase inhibitor can also be administered in combination with non-steroidal anti-inflammatory agents such as aspirin (acetylsalicylic acid), indomethacin, ibuprofen, naproxen, diclofenac, sulindac, oxaprozin, diflunisal, bromfenac, piroxicam, etodolac and fenoprofen. A HMG-CoA reductase inhibitor can additionally be used in combination with a leukotriene synthesis inhibitor or antagonist, including leukotriene receptor antagonists such as montelukast, pranlukast, zafirlukast and tomelukast, or with 5-lipoxygenase inhibitors such as zileuton (Drazen et al., N. Engl. J. Med. 340:197-206 (1999)). When a HMG-CoA reductase inhibitor is used with another anti-inflammatory agent, the HMG-CoA reductase inhibitor can generally be administered at a lower dosage. For example, a HMG-CoA reductase inhibitor can be administered at a dose of less than 0.1 mg per day in combination with another anti-inflammatory agent.

Physicians' Desk Reference

PRODUCT NAME

Brands containing: **MONTELUKAST SODIUM**

Singulair Tablets (Merck)

Singulair Chewable Tablets (Merck)

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Physicians' Desk Reference

PRODUCT NAME

Brands containing: **ZAFIRLUKAST**

Accolate Tablets (AstraZeneca)

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PDR® entry for

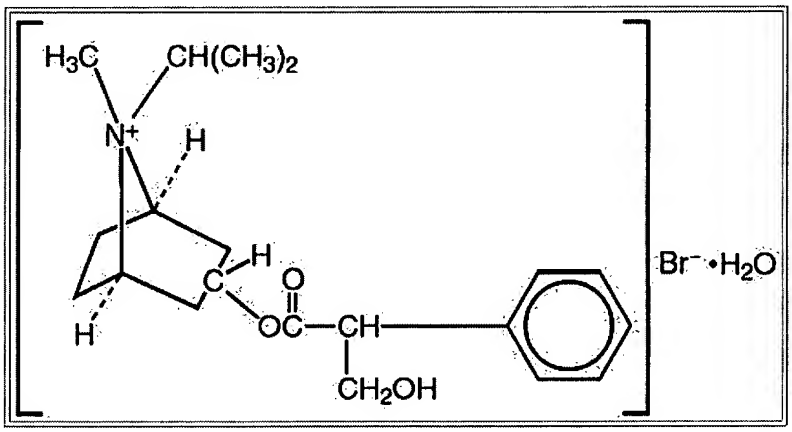
COMBIVENT® (Boehringer Ingelheim)
(ipratropium bromide and albuterol sulfate)

Inhalation Aerosol
Bronchodilator Aerosol
For Oral Inhalation Only
Prescribing Information

Description

DESCRIPTION

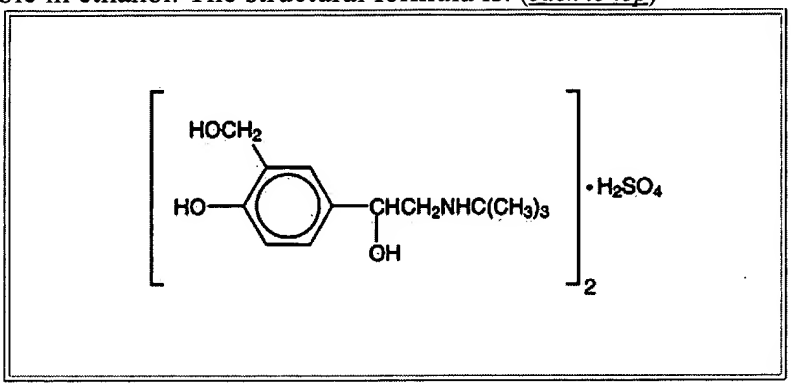
Combivent ® Inhalation Aerosol is a combination of ipratropium bromide and albuterol sulfate. Ipratropium bromide is an anticholinergic bronchodilator chemically described as 8-azoniabicyclo[3.2.1]octane, 3-(3-hydroxy-1-oxo-2-phenylpropoxy)- 8-methyl- 8-(1-methylethyl)-, bromide, monohydrate *(endo,syn)* -,(±): a synthetic quaternary ammonium compound chemically related to atropine. Ipratropium bromide is a white to off-white crystalline substance, freely soluble in water and lower alcohols but insoluble in lipophilic solvents such as ether, chloroform and fluorocarbons. The structural formula is:



$C_{20}H_{30}BrNO_3 \cdot H_2O$ ipratropium bromide Mol. Wt. 430.4

Albuterol sulfate, chemically known as (1,3-benzenedimethanol, (alpha)'-[[(1,1-dimethylethyl) amino] methyl]-4-hydroxy, sulfate (2:1)(salt), (±)- is a relatively selective beta $_2$ -adrenergic bronchodilator. Albuterol is the official generic name in the United States. The World Health Organization recommended name for the drug is salbutamol. Albuterol sulfate is a white to off-white crystalline powder, soluble in

water and slightly soluble in ethanol. The structural formula is: (*back to top*)



$(C_{13}H_{21}NO_3)_2 \cdot H_2SO_4$ albuterol sulfate Mol. Wt. 576.7

Combivent ® Inhalation Aerosol contains a microcrystalline suspension of ipratropium bromide and albuterol sulfate in a pressurized metered-dose aerosol unit for oral inhalation administration. The 200 inhalation unit has a net weight of 14.7 grams. Each actuation meters 21 mcg of ipratropium bromide and 120 mcg of albuterol sulfate from the valve and delivers 18 mcg of ipratropium bromide and 103 mcg of albuterol sulfate (equivalent to 90 mcg albuterol base) from the mouthpiece. The excipients are dichlorodifluoromethane, dichlorotetrafluoroethane, and trichloromonofluoromethane as propellants and soya lecithin.

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CLINICAL PHARMACOLOGY

Combivent ® Inhalation Aerosol is a combination of the anticholinergic bronchodilator, ipratropium bromide, and the beta $_2$ -adrenergic bronchodilator, albuterol sulfate.

Ipratropium Bromide:

Mechanism of Action

Ipratropium bromide is an anticholinergic (parasympatholytic) agent which, based on animal studies, appears to inhibit vagally mediated reflexes by antagonizing the action of acetylcholine, the transmitter agent released from the vagus nerve. Anticholinergics prevent the increases in intracellular concentration of cyclic guanosine monophosphate (cyclic GMP) which are caused by interaction of acetylcholine with the muscarinic receptor on bronchial smooth muscle.

Pharmacokinetics

The bronchodilation following inhalation of ipratropium bromide is primarily a local, site-specific effect, not a systemic one. Much of an administered dose is swallowed as shown by fecal excretion studies. Ipratropium bromide is a quaternary amine. It is not readily absorbed into the systemic circulation either from the surface of the lung or from the gastrointestinal tract as confirmed by blood level and renal excretion studies. Plasma levels of ipratropium bromide were below the assay sensitivity limit of 100 pg/mL.

The half-life of elimination is about 2 hours after inhalation or intravenous administration. Ipratropium

bromide is minimally bound (0 to 9% *in vitro*) to plasma albumin and (alpha) $_1$ -acid glycoprotein. It is partially metabolized to inactive ester hydrolysis products. Following intravenous administration, approximately one-half of the dose is excreted unchanged in the urine. Studies in rats have shown that ipratropium bromide does not penetrate the blood-brain barrier. The pharmacokinetics of Combivent ® Inhalation Aerosol or ipratropium bromide have not been studied in patients with hepatic or renal insufficiency or in the elderly (See PRECAUTIONS).

Controlled clinical studies have demonstrated that ipratropium bromide does not alter either mucociliary clearance or the volume or viscosity of respiratory secretions. In studies without a positive control, ipratropium bromide did not alter pupil size, accommodation or visual acuity (See ADVERSE REACTIONS).

Ventilation/perfusion studies have shown no clinically significant effects on pulmonary gas exchange or arterial oxygen tension. At recommended doses, ipratropium bromide does not produce clinically significant changes in pulse rate or blood pressure.

Albuterol Sulfate:

Mechanism of Action

In-vitro studies and *in-vivo* pharmacologic studies have demonstrated that albuterol has a preferential effect on beta $_2$ -adrenergic receptors compared with isoproterenol. While it is recognized that beta $_2$ -adrenergic receptors are the predominant receptors on bronchial smooth muscle, recent data indicate that there is a population of beta $_2$ -receptors in the human heart which comprise between 10% and 50% of cardiac beta-adrenergic receptors. The precise function of these receptors, however, is not yet established (See WARNINGS).

Activation of beta $_2$ -adrenergic receptors on airway smooth muscle leads to the activation of adenylyl cyclase and to an increase in the intracellular concentration of cyclic-3',5'-adenosine monophosphate (cyclic AMP). This increase of cyclic AMP leads to the activation of protein kinase A, which inhibits the phosphorylation of myosin and lowers intracellular ionic calcium concentrations, resulting in relaxation. Albuterol relaxes the smooth muscles of all airways, from the trachea to the terminal bronchioles. Albuterol acts as a functional antagonist to relax the airway irrespective of the spasmogen involved, thus protecting against all bronchoconstrictor challenges. Increased cyclic AMP concentrations are also associated with the inhibition of release of mediators from mast cells in the airway.

Albuterol has been shown in most clinical trials to have more bronchial smooth muscle relaxation effect than isoproterenol at comparable doses while producing fewer cardiovascular effects. However, all beta-adrenergic drugs, including albuterol sulfate, can produce a significant cardiovascular effect in some patients (See PRECAUTIONS).

Pharmacokinetics

Albuterol is longer acting than isoproterenol in most patients because it is not a substrate for the cellular uptake processes for catecholamines nor for metabolism by catechol-O-methyl transferase. Instead, the drug is conjugatively metabolized to albuterol 4'-O-sulfate.

In a pharmacokinetic study in 12 healthy male volunteers of two inhalations of albuterol sulfate, 103 mcg dose/inhalation through the mouthpiece, peak plasma albuterol concentrations ranging from 419 to 802

PDR® entry for

ATROVENT® (Boehringer Ingelheim)

(ipratropium bromide)

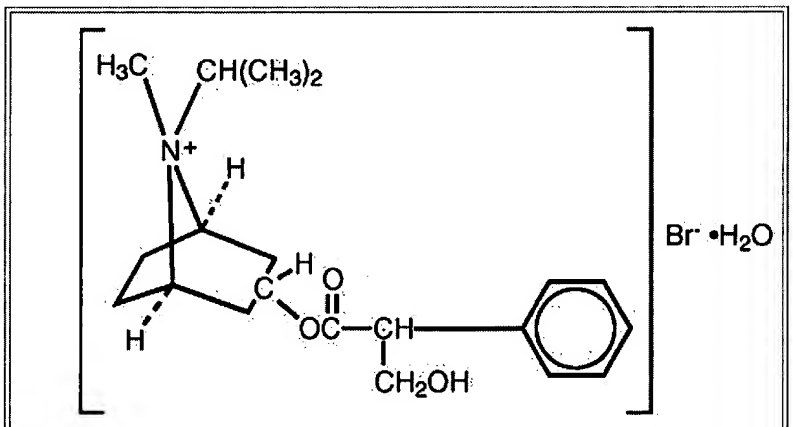
Inhalation Aerosol
Bronchodilator BI-CODE 82

Description

Prescribing Information

DESCRIPTION

The active ingredient in Atrovent ® (ipratropium bromide) Inhalation Aerosol is ipratropium bromide. It is an anticholinergic bronchodilator chemically described as 8-azoniabicyclo (3.2.1)-octane,3-(3-hydroxy-1-oxo-2-phenylpropoxy)-8-methyl-8- (1-methylethyl)-, bromide, monohydrate *(endo, syn)-*, (±)-: a synthetic quaternary ammonium compound, chemically related to atropine.



ipratropium bromide (Atrovent)
$C_{20}H_{30}BrNO_3 \cdot H_2O$
Mol. Wt. 430.4

Ipratropium bromide is a white crystalline substance, freely soluble in water and lower alcohols but insoluble in lipophilic solvents such as ether, chloroform, and fluorocarbons.

Atrovent Inhalation Aerosol is an inhalation aerosol for oral administration. The net weight is 14 grams; it yields 200 inhalations. Each actuation of the valve delivers 18 mcg of ipratropium bromide from the mouthpiece. The inert ingredients are dichlorodifluoromethane, dichlorotetrafluoroethane, and

trichloromonofluoromethane as propellants and soya lecithin.

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CLINICAL PHARMACOLOGY

Atrovent ® (ipratropium bromide) is an anticholinergic (parasympatholytic) agent which, based on animal studies, appears to inhibit vagally mediated reflexes by antagonizing the action of acetylcholine, the transmitter agent released from the vagus nerve. Anticholinergics prevent the increases in intracellular concentration of cyclic guanosine monophosphate (cyclic GMP) which are caused by interaction of acetylcholine with the muscarinic receptor on bronchial smooth muscle.

The bronchodilation following inhalation of Atrovent is primarily a local, site-specific effect, not a systemic one. Much of an inhaled dose is swallowed as shown by fecal excretion studies. Atrovent is not readily absorbed into the systemic circulation either from the surface of the lung or from the gastrointestinal tract as confirmed by blood level and renal excretion studies.

The half-life of elimination is about 2 hours after inhalation or intravenous administration. Autoradiographic studies in rats have shown that Atrovent does not penetrate the blood-brain barrier.

In controlled 90 day studies in patients with bronchospasm associated with chronic obstructive pulmonary disease (chronic bronchitis and emphysema) significant improvements in pulmonary function (FEV_1 and $FEF_{25-75\%}$ increases of 15% or more) occurred within 15 minutes, reached a peak in 1-2 hours, and persisted for periods of 3 to 4 hours in the majority of patients and up to 6 hours in some patients. In addition, significant increases in Forced Vital Capacity (FVC) have been demonstrated.

Controlled clinical studies have demonstrated that Atrovent ® (ipratropium bromide) does not alter either mucociliary clearance or the volume or viscosity of respiratory secretions. In studies without a positive control Atrovent did not alter pupil size, accommodation or visual acuity (See ADVERSE REACTIONS).

Ventilation/perfusion studies have shown no clinically significant effects on pulmonary gas exchange or arterial oxygen tension. Atrovent does not produce clinically significant changes in pulse rate or blood pressure.

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INDICATIONS AND USAGE

Atrovent ® (ipratropium bromide) Inhalation Aerosol is indicated as a bronchodilator for maintenance treatment of bronchospasm associated with chronic obstructive pulmonary disease, including chronic bronchitis and emphysema.

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CONTRAINDICATIONS

Atrovent ® (ipratropium bromide) Inhalation Aerosol is contraindicated in patients with a history of hypersensitivity to soya lecithin or related food products such as soybean and peanut. Atrovent should also not be taken by patients hypersensitive to any other components of the drug product or to atropine or its